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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,643	10/31/2001	Bradley T. Hyman	19603/3541 (CRF D-2694A)	2817
7590	01/26/2005		EXAMINER	
Michael L. Goldman NIXON PEABODY LLP Clinton Square P.O. Box 31051 Rochester, NY 14603			MANTIS MERCADER, ELENI M	
			ART UNIT	PAPER NUMBER
			3737	
DATE MAILED: 01/26/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

8N

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	10/001,643		HYMAN ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Eleni Mantis Mercader		3737	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 08 November 2004.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>11/08/2004</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Response to Arguments***

Applicant's arguments filed on 09/10/2004 have been fully considered but they are not persuasive. With respect to the prior art the rejection is still applicable because the Applicant is arguing the lack of steps in the prior art, which are not currently claimed by the current invention. By Applicant's own Declaration it appears that all of these steps are required in combination in order for the invention to function. Therefore, since the current independent claims do not claim all these steps, then the current claims are incomplete and inoperable.

### ***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-34 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: using a thin skull, using the particular wavelength required for multiphoton excitation, using the required power level and pulsed durations and the summing of the low energy photons.

### ***Claim Rejections - 35 USC § 101***

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Art Unit: 3737

4. Claims 1-34 are rejected under 35 U.S.C. 101 because the disclosed invention is inoperative and therefore lacks utility. The claimed subject matter does not claim the required steps for the invention to be operable. As per applicant's own admission in order for the invention to be operable the following steps are required: using a thin skull, using the particular wavelength required for multiphoton excitation, using the required power level and pulsed durations and the summing of the low energy photons.

*Claim Rejections - 35 USC § 112*

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-34 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The steps of using a thin skull, using the particular wavelength required for multiphoton excitation, using the required power level and pulsed durations and the summing of the low energy photons are critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). As per applicant's own admission in the Declaration of 9/10/2004, in order for the invention to be enabled the following steps are required: using a thin skull, using the particular wavelength required for multiphoton excitation, using the required power level and pulsed durations and the summing of the low energy photons. Therefore, these steps must be claimed.

*Claim Rejections - 35 USC § 103*

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gervais et al.'717 in view of Alfano et al.'386 and Christie et al. (Abstract published in Society of Neuroscience Abstracts 1998).

Gervais et al.'717 teach a method of detecting neurodegenerative diseases by detecting amyloid plaques or neurofibrillary tangles in a mammal by activating the tissue of interest, including the brain, in-vivo and by using optical imaging under conditions effective to promote a fluorescence characteristic in order to diagnose amyloidosis related diseases such as Alzheimer's in early stages (see paragraphs 9-12, 35 and 156; describing detecting fluorescence to optically image the brain in order to diagnose diseases such as Alzheimer's).

While Gervais et al.'717 do not explicitly teach comparing the fluorescence characteristic to a standard fluorescence emitted by exciting healthy brain tissue of the mammal under the same conditions used to carryout the activating, it is well within the knowledge of skilled artisans that there has to be some type of comparison to a standard in order to determine the significance of what is being identified in the image. In other words, if there is a luminous site in the image, either comparison with a normal image or some other type of normalization will be undertaken to ensure that what is being observed is of significance. Such image processing is described by

Art Unit: 3737

Alfano et al.'386, in col. 6, lines 17-52, wherein subtraction between images and normalization is undertaken in order to obtain a better image and thereby allow diagnosis of disease.

Photo-activation by laser and pulsed radiation are well known imaging expedients to skilled artisans.

Gervais et al.'717 in view of Alfano et al.'386 do not explicitly teach multiphoton excitation to detect neurodegenerative diseases.

In the same field of endeavor, Christie et al. (Society of Neuroscience Abstracts 1998) teach multiphoton excitation to detect neurodegenerative diseases such as Alzheimer's to enhance the ability to image amyloids deep within the living tissues by using fluorophores.

Therefore, it would have been obvious to one skilled in the art at the time that the invention was made to have modified Gervais et al.'717 in view of Alfano et al.'386 to incorporate the teachings of Christie et al. in using multiphoton excitation as that improves the imaging of amyloids deep within the tissue.


With respect to the use of a "thin" skull, it would have been obvious to one skilled in the art at the time that the invention was made that Christie et al. do thin the skull since the abstract refers to gathering information from brain tissue and if there was intervening bone structure, Christie et al. would not have been able to gather any data.

Art Unit: 3737

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eleni Mantis Mercader whose telephone number is (571) 272-4740. The examiner can normally be reached on Mon. - Fri., 8:00 a.m.-6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Casler can be reached on (571) 272-4956. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Eleni Mantis Mercader  
Primary Examiner  
Art Unit 3737

EMM